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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/180,340	08/20/1999	NANCY W.Y. HO	7024109PUR48	6674

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EXAMINER

ROBINSON, HOPE A

ART UNIT	PAPER NUMBER
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1653

DATE MAILED: 10/02/2003

21

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/180,340

Applicant(s)

HO ET AL.

Examiner

Hope A. Robinson

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 30 June 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-34 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☐ Claim(s) 1-34 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other:

DETAILED ACTION

1. Applicant's response to the Office Action mailed March 27, 2003 in Paper No. 22 on June 30, 2003 is acknowledged.
2. Claims 1, 14, 18, 23, 25, 27 and 30 have been amended. Claims 1-34 are pending and under examination.
3. The following grounds of rejection are or remain applicable:

Claim Rejections - 35 U.S.C. § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 22-28 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 25 is indefinite for the recitation of "substantially retaining its capacity for fermenting xylose to ethanol", how much is considered to be "substantial retention" as the term is not defined in the specification (see also claims 22-23 and the dependent claims hereto).

Claim 28 is indefinite for the recitation of "second section marker" instead of "second selection marker".

5. Applicant's arguments filed June 30, 2003 in Paper No. 22 has been considered. The response on page 5 states that the examiner fails to provide any legal support for the rejection

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and the rejection is without basis with regard to claim 25. The response further states that if the "examiner is stating that a bright-line test must be provided to define the use of a relative term in a claim, the courts have repeatedly held that this is not required by the law". Applicant's assertions are incorrect. What is required is a clear meaning of the term "substantially retaining" with regard the function recited in the claim, as the metes and bounds of the claim is undefined with this terminology. The specification does not rectify this situation as the term is not defined in the specification, thus one of skill the art would not be able to ascertain what is considered to be a "substantially retaining the capacity for fermenting xylose to ethanol when cultured under non-selective conditions". Can the yeast ferment xylose to ethanol for 20 generations following culture under non-selective conditions? It is suggested that "substantially" is deleted from the claim. Note that the typo of "second section marker" remains in the claim, although applicant's response state that it has been corrected. Therefore, applicant's arguments are not persuasive.

Claim Rejections - 35 U.S.C. § 103

The following is a quotation of 35 U.S.C. 103 (a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

6. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103 (a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103 (c) and potential 35 U.S.C. 102 (f) or (g) prior art under 35 U.S.C. 103 (a).

7. Claims 1-13, 23-29, 31 and 34 remain rejected under 35 U.S.C. 103(a) as obvious over Ho et al. (WO95/13362, May 18, 1995) in view of Hallborn et al. (CA 2090122, October 17, 1991).

Ho et al. teach recombinant yeasts containing genes encoding xylose reductase, xylitol dehydrogenase and xylulokinase, and DNA molecules, vectors and methods useful for producing such yeasts (see claim 1 of the instant invention). The recombinant yeasts effectively ferment xylose to ethanol, and preferred yeasts are capable of simultaneously fermenting glucose and xylose to ethanol (see claims 1 and 2 of the instant invention and the abstract and page 3 of the reference). The reference teach the fermentation of glucose to ethanol via the yeast *Saccharomyces* (see claim 3 of the instant invention and pages 3-5 of the reference). Ho et al. indicate that the yeast of the invention can ferment the two sugars (xylose and glucose) to ethanol simultaneously achieved where the xylitol dehydrogenase, xylulokinase and xylose reductase genes are fused to promoters which are not inhibited by the presence of glucose and also do not require xylose for induction (see page 6 of the reference and claims 5-8 of the instant invention). In addition, the recombinant yeast strain containing xylitol dehydrogenase, xylulokinase and xylose reductase genes are fused to non-glucose-inhibited promoters and the

yeast is capable of fermenting xylose to ethanol and glucose to ethanol (see pages 6-7 and claim 9 of the instant invention).

Ho et al. teach direct amplification of the intact xylitol dehydrogenase gene and the promoter less xylitol dehydrogenase from *Pichia stipitis* chromosomal DNA (see Figure 10 and page 10). Furthermore, Ho et al. disclose that suitable sources of xylitol dehydrogenase, and xylose reductase genes include xylose-utilizing yeasts such as *Candida shehatae*, *Pichia stipitis*, *Pachysolen tannophilus* and suitable sources of xylulokinase genes include the above yeasts as well as xylose non-utilizing yeasts such as those from genus *Saccharomyces cerevisiae*, *Schizosaccharomyces pombe* and bacteria such as *Escherichia coli* etc. (see page 13 and claims 10-12 of the instant invention). Additionally, the reference teaches selection markers in *S. cerevisiae* (see pages 15 and 16) and specific DNA fragments that serve as the replicon and selection markers that enable the plasmid to be replicated autonomously in *S. cerevisiae*. Further, it is disclosed that the yeast transformants containing the plasmid is distinguished from the untransformed host cells (see page 16). In-so-far-as Ho et al. do not explicitly teach the integration at multiple sites, Hallborn et al. teach recombinant yeasts that ferments xylose to ethanol, having genes integrated (multicopies) into the yeast chromosome. The genes taught by Hallborn et al. encode xylose reductase and xylitol dehydrogenase. Hallborn et al. also teach a yeast from *Saccharomyces* and a method of transforming cells with integrative plasmids (see pages 1-9 of the reference).

Therefore, it would have been obvious to one of ordinary skill in the art to arrive at the claimed invention as a whole because Ho et al. and Hallborn et al. teach the fermentation of sugars to ethanol (i.e. xylose and glucose) using the same strain of yeast. One of skill in the art would reasonable expect successful results by combining the two references because Hallborn et al. teach integrative plasmids and an autonomously replicating plasmid suitable for carrying out transformation stably. Moreover, one of skill in the art would be motivated to combine the

teachings of the references because Ho et al. disclose that ethanol is an ideal liquid fuel for automobiles and Hallborn et al. disclose a method to perform stable transformations over time. Therefore, the claimed invention was *prima facie* obvious.

8. Applicant's arguments filed June 30, 2003 in Paper No. 22 has been considered. The response on pages 7+ provides a general summary of the Ho et al. and Hallborn et al. references and it is stated that Hallborn et al. "do not teach or suggest the introduction of a gene encoding xylulokinase, and stat that both *S. cerevisiae* and *Sch. Pombe* have a functioning xylulokinase gene", therefore, the combined teachings of the references remains pertinent to the claimed invention by admission by applicant. Note that claim 1 does not require the introduction of a gene encoding xylulokinase and applicant's statements acknowledges that the reference teaches a functioning xylulokinase gene. Hence this argument is not persuasive. Applicant also state that there is no motivation to combine the two references, however, this statement is not accurate as both references teach the fermentation of xylose to ethanol and the use of the claimed enzymes (see claim 1 for example). On page 10 of the response applicant states that none of the references teach the product plasmid vector, yet on page 8 the statement is made that "Hallborn et al. teach integration of foreign DNA into the yeast genome.... An autonomously replicating plasmid is also introduced....". Thus applicant's arguments are inconsistent and contradictory. Therefore, the rejection remains for the reasons stated above. Note that the rejection over the method claims has been withdrawn.

9. Claims 1-34 remain rejected under 35 U.S.C. 103(a) as obvious over Ho et al. (WO95/13362, May 18, 1995) in view of Lopes et al. (Yeast, vol. 12, no.5, pages 467-477, April 1996).

Ho et al. teach recombinant yeasts containing genes encoding xylose reductase, xylitol dehydrogenase and xylulokinase, and DNA molecules, vectors and methods useful for producing such yeasts (see claim 1 of the instant invention). The recombinant yeasts effectively ferment xylose to ethanol, and preferred yeasts are capable of simultaneously fermenting glucose and xylose to ethanol (see claims 1 and 2 of the instant invention and the abstract and page 3 of the reference). The reference teach the fermentation of glucose to ethanol via the yeast *Saccharomyces* (see claim 3 of the instant invention and pages 3-5 of the reference). Ho et al. indicate that the yeast of the invention can ferment the two sugars (xylose and glucose) to ethanol simultaneously achieved where the xylitol dehydrogenase, xylulokinase and xylose reductase genes are fused to promoters which are not inhibited by the presence of glucose and also do not require xylose for induction (see page 6 of the reference and claims 5-8 of the instant invention). In addition, the recombinant yeast strain containing xylitol dehydrogenase, xylulokinase and xylose reductase genes are fused to non-glucose-inhibited promoters and the yeast is capable of fermenting xylose to ethanol and glucose to ethanol (see pages 6-7 and claim 9 of the instant invention).

Ho et al. teach direct amplification of the intact xylitol dehydrogenase gene and the promoter less xylitol dehydrogenase from *Pichia stipitis* chromosomal DNA (see Figure 10 and page 10). Furthermore, Ho et al. disclose that suitable sources of xylitol dehydrogenase, and xylose reductase genes include xylose-utilizing yeasts such as *Candida shehatae*, *Pichia stipitis*, *Pachysolen tannophilus* and suitable sources of xylulokinase genes include the above yeasts as well as xylose non-utilizing yeasts such as those from genus *Saccharomyces cerevisiae*, *Schizosaccharomyces pombe* and bacteria such as *Escherichia coli* etc. (see page 13 and claims 10-12 of the instant invention). Additionally, the reference teaches selection markers in *S. cerevisiae* (see pages 15 and 16) and specific DNA fragments that serve as the replicon and selection markers that enable the plasmid to be replicated autonomously in *S. cerevisiae*.

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Further, it is disclosed that the yeast transformants containing the plasmid is distinguished from the untransformed host cells (see page 16). In-so-far-as Ho et al. do not explicitly teach integrative or replicative plasmids, Lopes et al. teach numerous plasmids containing various genes integrated into a ribosomal RNA gene of *Saccharomyces cerevisiae*. Multiple copies of the plasmid were successfully integrated into the genome (over 140 copies); which are stably maintained in non-selective medium for multiple generations over long periods of time (see abstract and pages 467-475). Further, the plasmids contained a Leu2d selection marker and various cloned genes for stability and expression studies. Yeast transformants were selected by plating on agar plates containing yeast nitrogen base (without amino acids), glucose and histidine. The same medium was used for growing the transformants in liquid culture (see page 468 and Figure 1 and see claims 14-33).

Therefore, It would have been obvious to one of ordinary skill in the art to arrive at the claimed invention as a whole by combining the teachings of Ho et al. and Lopes et al. because Ho et al. teach that the simultaneous fermentation of xylose and glucose into ethanol from the yeast *Saccharomyces cerevisiae*, as ethanol is said to be an ideal liquid fuel for automobiles and Lopes teach a method of making transformants stably maintained in non-selective medium for multiple generations over long periods of time. One of ordinary skill in the art would be motivated to combine the teachings of both references because the method taught by Ho et al. introduces DNA into the same yeast taught by Lopes et al. Thus, the claimed invention was obvious to make and use at the time it was made and was *prima facie* obvious.

10. Applicant's arguments filed June 30, 2003 in Paper No. 22 has been considered. Applicant contends that Lopes et al. do not teach the claimed invention and that there is no motivation to combine the references. Ho et al. has already been addressed above. Regarding Lopes et al. the reference shows in Figure 1 plasmids that contain not only the Leu2d selection

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marker but also various cloned genes for stability and expression studies. In addition on page 468, paragraph 1, it is disclosed that "yeast transformants were selected by plating.... The same medium was used for growing the transformants in liquid culture". In addition, the Lopes et al. reference is not to be analyzed on its own as the combined teaching of Ho et al. taken with Lopes et al. renders the claimed invention as obvious. Thus, the claimed invention is obvious for the reasons stated above.

Conclusion

11. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

12. No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Hope Robinson whose telephone number is (703) 308-6231. The


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examiner can normally be reached on Monday and Wednesday-Friday from 9:00 am to 5:30 pm (EST).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher S.F. Low, can be reached at (703) 308-2923.

Any inquiries of a general nature relating to this application should be directed to the Group Receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted by facsimile transmission. The official fax phone number for Technology Center 1600 is (703) 308-4242. Please affix the examiner's name on a cover sheet attached to your communication should you choose to fax your response. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG (November 15, 1989).


Hope Robinson, MS

Patent Examiner



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